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REMARKS

Claims 1-94 are pending in this application. Claim 1 has been amended to replace the term "CHR²" in the definition of variable "W" with the term "CHR⁵⁰". Support for new variable R⁵⁰ can be found in the definition of R². Claim 1 also has been amended to correct language the Office Action deemed inappropriate. Support can be found in claim 1 as filed. No new matter has been added. Claim 42 has been rewritten as new claim 95 to remove superfluous language. Claim 41 has been amended to recite the substituent variables of Table 8. Claims 64 and 73 have been amended to delete reference to "preventing" prostate disorders. No new matter has been added.

As a preliminary matter, Applicants wish to thank Examiners Wright and Chang for the courtesy afforded Applicants' undersigned attorney and Mr. Eric Voelk in a telephonic interview held on September 5, 2002. In the interview, the species election levied in this application was discussed. Applicants' undersigned attorney and Mr. Voelk were informed that the search conducted pursuant to the species election included embodiments wherein ring "J" was a three to seven membered ring containing oxygen, and substituents on such ring according to the claims. Applicants' undersigned attorney and Mr. Voelk were further informed that in the event the present art-based rejections of record were overcome, the search would be expanded to include certain other ring "J" embodiments, such as to be agreed upon a later date.

Claims 1-58 and 60 are rejected for alleged obviousness-type double patenting over claims 1-18 of U.S. Patent 5,808,060 ("the 060 patent"), on the basis that the 060 patent teaches a genus that embraces the genus of the present claims. Specifically, the Office Action asserts that variable "X" of the 060 patent is broader than the allegedly corresponding variables "Q" and "W" of the present application, and that motivation to achieve the present claims exists on the basis that the compounds of the 060 patent are similar in structure, and have the same method of use. Applicants respectfully request reconsideration of the rejection.



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The present claims require that variable R^7 or R^{7a} (which includes ring J) must be present at substituent Q or W of the claimed genus. In contrast, the genus of the 060 patent contains no such limitation. Rather, variable "X" of the 060 patent (which appears at positions corresponding to both variables Q and W of the present claims) can be independently unsubstituted alkylene, substituted alkylene, a monosaccharide of 5-7 carbons having certain recited hydroxyl substitutions, or one of a list of functional groups. Nowhere in the 060 patent is it taught to require an "X" variable to be the structure of variable R^7 or R^{7a} of the present claims. Indeed, to achieve the presently claimed invention, those of ordinary skill in the art would have to engage in impermissible picking and choosing among the possibilities of the 060 patent, necessarily using the present specification as a template. As will be appreciated, an obviousness rejection cannot be based upon such a basis. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1-58 and 60 are rejected under 35 U.S.C. § 103(a) for alleged obviousness over International Application WO 98/07433 to Sauliner et al. ("the Sauliner reference"). The Office Action asserts that:

The difference between the Sauliner et al. reference and the instant claims is that Sauliner et al. generically teach " CH_2 " for the "W" in the instant claims. See Sauliner et al., page 18, compound Ib, and the Q variables in Table V on pages 60-62.

Office Action at page 5. However, the Sauliner et al. genus requires that position 13 of its disclosed ring system (corresponding to variable "Q" of the present claims) be a nitrogen atom bearing one of a hydrogen atom, a pentose group A, or a hexose group B. See Sauliner et al. at page 4. The Sauliner et al. genus further requires that its variable "Q" (corresponding to variable "W" of the present claims) be only O, S, NR_5 , or CH_2 . Thus, the Sauliner et al. reference requires O, S, substituted nitrogen or methylene at the position corresponding to "W" of the present claims, whereas the present genus recites that variable "W" be a *substituted carbon moiety* (specifically, CHR_{50} or $CR_{18}R_7$).

The Office Action further asserts that:



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One having ordinary skill in the art would be motivated to prepare a compound wherein W is CR18R17 in the claims because Sauliner et al. generically teach that the "W" moiety can optionally be O, S or CH₂. Variation of the "W" moiety has been exemplified to have similar activity, see table V in the instant claims. It would be expected by a person having ordinary skill in the art that the other options generically taught by Sauliner et al. would have similar activity.

Office Action at page 6. However, the embodiments in Table V of Sauliner et al. pointed to by the Office Action possess **only** O, S or NH at position Q. Indeed, there is **no** disclosure or suggestion in Sauliner et al. of any substituted carbon moiety at this position, and Applicants do not find in Sauliner any disclosure of **any** specific compound having **any** substitution at this position, let alone the substituted carbon moieties of the present claims.¹ Accordingly, Applicants respectfully assert that the present claims cannot be found obvious over the Sauliner et al. reference.

Claims 64 and 73 are rejected under 35 U.S.C. § 112, first paragraph on the basis that "preventing prostate disorders" is not enabled. While Applicants disagree with the Office Action, and assert that the present specification provides ample guidance for making and using the present invention, solely in an effort to advance prosecution Applicants have amended the claims to remove the reference to "preventing" prostate disorders.

Claims 1, 2 and 41 are rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness for reciting language that the Office Action considered indefinite. Applicants believe that the rejection has been overcome by the present amendment to claim 1.

The Office Action further questions the phrase "carbon atom that is saturated". While the Office Action is correct that "saturation" refers to the lack of double or triple bonds, the term "saturated carbon atom" is well known to those of skill in the art to mean a carbon atom that does not participate in such a double or triple bond. For example, those of skill in the art would

¹ Applicants note that the genus shown on page 4 of the Sauliner et al. reference indicates that variable "R_{1a}" can be attached to "Q", and can be "pentose group (A)" or "hexose group (B)". However, no such embodiment is presented in Sauliner et al., and, as discussed above, the Sauliner et al. disclosure explicitly limits the definition of "Q" to O, S, NR₂ or CH₂.



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recognize the compound cyclopentene to be a 5-membered cyclic hydrocarbon possessing one double bond, and three saturated carbon atoms. Cyclopentadiene would similarly be recognized to possess two double bonds and one saturated carbon atom. Inasmuch as those of skill in the art would understand the present claim language, Applicants respectfully assert that the present claim language is proper within the patent laws.

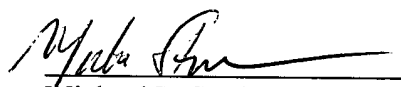
The Office Action also questions claim 41 for the reference to the substituents of Table 8. Applicants have amended claim 41 to recite the Table 8 substituents explicitly.

Applicants thank the Examiner for pointing out the superfluous language in claim 42. Applicants have rewritten the claim as new claim 95, which does not contain the questioned language.

In view of the foregoing, Applicant submits that the claims as amended are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **A Version with markings to show changes made.**

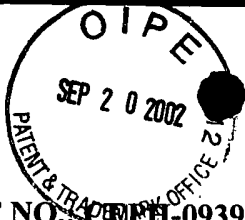
Respectfully submitted,


Michael P. Straher
Registration No. 38,325

Date: September 20, 2002

WOODCOCK WASHBURN LLP
One Liberty Place B 46th Floor
Philadelphia, PA 19103
(215)568-3100

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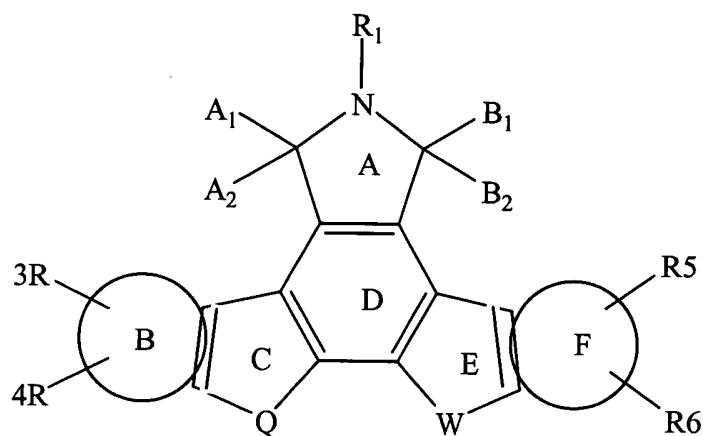
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 42 has been deleted.

Claims 1, 41, 64 and 73 have been amended as shown below:

1. (Once Amended) A compound having the Formula I:



wherein:

ring B and ring F, independently, and each together with the carbon atoms to which they are attached, are selected from the group consisting of:

- an unsaturated 6-membered carbocyclic aromatic ring in which from 1 to 3 carbon atoms may be replaced by nitrogen atoms; and
- an unsaturated 5-membered carbocyclic aromatic ring; [and
- an unsaturated 5-membered carbocyclic aromatic ring] in which, optionally, either

- one carbon atom is replaced with an oxygen, nitrogen, or sulfur atom;
- two carbon atoms are replaced with a sulfur and a nitrogen atom, an oxygen and a nitrogen atom, or two nitrogen atoms; or

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3) three carbon atoms are replaced with three nitrogen atoms;

R^1 is selected from the group consisting of:

- a) H, substituted or unsubstituted alkyl having from 1 to 4 carbons, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, or substituted or unsubstituted heteroarylalkyl;
- b) $-C(=O)R^9$, where R^9 is selected from the group consisting of alkyl, aryl and heteroaryl;
- c) $-OR^{10}$, where R^{10} is selected from the group consisting of H and alkyl having from 1 to 4 carbons;
- d) $-C(=O)NH_2$, $-NR^{11}R^{12}$, $-(CH_2)_pNR^{11}R^{12}$, $-(CH_2)_pOR^{10}$, $-O(CH_2)_pOR^{10}$ and $-O(CH_2)_pNR^{11}R^{12}$, wherein p is from 1 to 4; and wherein either

1) R^{11} and R^{12} are each independently selected from the group consisting of H and alkyl having from 1 to 4 carbons; or

2) R^{11} and R^{12} together form a linking group of the formula $-(CH_2)_2-X^1-(CH_2)_2-$, wherein X^1 is selected from the group consisting of $-O-$, $-S-$, and $-CH_2-$;

R^2 is selected from the group consisting of H, alkyl having from 1 to 4 carbons,

$-OH$, alkoxy having from 1 to 4 carbons, $-OC(=O)R^9$, $-OC(=O)NR^{11}R^{12}$, $-O(CH_2)_pNR^{11}R^{12}$, $-O(CH_2)_pOR^{10}$, substituted or unsubstituted arylalkyl having from 6 to 10 carbons, and substituted or unsubstituted heteroarylalkyl;

R^3 , R^4 , R^5 and R^6 are each independently selected from the group consisting of:

- a) H, aryl, heteroaryl, F, Cl, Br, I, $-CN$, CF_3 , $-NO_2$, $-OH$, $-OR^9$, $-O(CH_2)_pNR^{11}R^{12}$, $-OC(=O)R^9$, $-OC(=O)NR^{11}R^{12}$, $-O(CH_2)_pOR^{10}$, $-CH_2OR^{10}$, $-NR^{11}R^{12}$, $-NR^{10}S(=O)_2R^9$, $-NR^{10}C(=O)R^9$,
- b) $-CH_2OR^{14}$, wherein R^{14} is the residue of an amino acid after the hydroxyl group of the carboxyl group is removed;
- c) $-NR^{10}C(=O)NR^{11}R^{12}$, $-CO_2R^2$, $-C(=O)R^2$, $-C(=O)NR^{11}R^{12}$, $-CH=NOR^2$, $-CH=NR^9$, $-(CH_2)_pNR^{11}R^{12}$, $-(CH_2)_pNHR^{14}$, or $-CH=NNR^2R^{2A}$ wherein R^{2A} is

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the same as R^2 ;

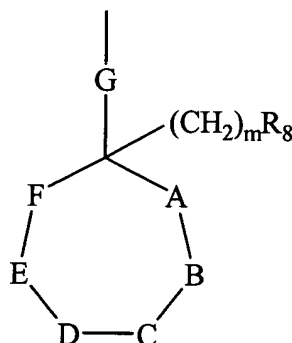
- d) $-S(O)_yR^2$, $-(CH_2)_pS(O)_yR^9$, $-CH_2S(O)_yR^{14}$ wherein y is 0, 1 or 2;
 e) alkyl having from 1 to 8 carbons, alkenyl having from 2 to 8 carbons, and alkynyl having 2 to 8 carbons, wherein

1) each alkyl, alkenyl, or alkynyl group is unsubstituted; or

2) each alkyl, alkenyl or alkynyl group is substituted with

1 to 3 groups selected from the group consisting of aryl having from 6 to 10 carbons, heteroaryl, arylalkoxy, heterocycloalkoxy, hydroxylalkoxy, alkyloxyalkoxy, hydroxyalkylthio, alkoxy-alkylthio, F, Cl, Br, I, -CN, -NO₂, -OH, -OR⁹, -X²(CH₂)_pNR¹¹R¹², -X²(CH₂)_pC(=O)NR¹¹R¹², -X²(CH₂)_pOC(=O)NR¹¹R¹², -X²(CH₂)_pCO₂R⁹, X²(CH₂)_pS(O)_yR⁹, -X²(CH₂)_pNR¹⁰C(=O)NR¹¹R¹², -OC(=O)R⁹, -OCONHR², -O-tetrahydropyranyl, -NR¹¹R¹², -NR¹⁰CO₂R⁹, -NR¹⁰C(=O)NR¹¹R¹², -NHC(=NH)NH₂, NR¹⁰C(=O)R⁹, -NR¹⁰S(O)₂R⁹, -S(O)_yR⁹, -CO₂R², -C(=O)NR¹¹R¹², -C(=O)R², -CH₂OR¹⁰, -CH=NNR²R^{2A}, -CH=NOR², -CH=NR⁹, -CH=NNHCH(N=NH)NH₂, -S(=O)₂NR²R^{2A}, -P(=O)(OR¹⁰)₂, -OR¹⁴, and a monosaccharide having from 5 to 7 carbons wherein each hydroxyl group of the monosaccharide is independently either unsubstituted or is replaced by H, alkyl having from 1 to 4 carbons, alkylcarbonyloxy having from 2 to 5 carbons, or alkoxy having from 1 to 4 carbons;

 X^2 is O, S, or NR¹⁰; R^7 is



wherein:

m is 0-4;

G is a bond; or alkylene having 1 to 4 carbons, wherein the alkylene group is unsubstituted, or substituted with $NR^{11A}R^{12A}$ or OR^{19} ;

R^{11A} and R^{12A} are the same as R^{11} and R^{12} ;

R^{19} is selected from the group consisting of H, alkyl, acyl, and

$C(=O)NR^{11A}R^{12A}$;

R^8 is selected from the group consisting of $O(C=O)NR^{11}R^{12}$, -CN, acyloxy, alkenyl, $-O-CH_2-O-(CH_2)_2-O-CH_3$, halogen and R^{1A} wherein R^{1A} is the same as R^1 ;

A and B are independently selected from the group consisting of O, N, S, CHR^{17} , $C(OH)R^{17}$, $C(=O)$, and $CH_2=C$; or A and B together can form $-CH=CH-$;

C and D are independently selected from the group consisting of a bond, O, N, S, CHR^{17} , $C(OH)R^{17}$, $C(=O)$ and $CH_2=C$;

E and F are independently selected from the group consisting of a bond, O, N, S, $C(=O)$, and $CH(R^{17})$;

R^{17} is selected from the group consisting of H, substituted or unsubstituted alkyl, alkoxycarbonyl, and substituted or unsubstituted alkoxy;

wherein:

- 1) ring J contains 0 to 3 ring heteroatoms;
- 2) any two adjacent hydroxyl groups of ring J can be joined in a

dioxolane ring;

3) any two adjacent ring carbon atoms of ring J can be joined to form a fused aryl or heteroaryl ring;

4) any two adjacent ring nitrogen atoms of ring J can be joined to form a fused heterocyclic ring which can be substituted with 1 to 3 alkyl or aryl groups;

provided that:

1) ring J contain at least one carbon atom that is saturated;

2) ring J not contain two adjacent ring O atoms;

3) ring J contains a maximum of two ring C(=O) groups;

4) when G is a bond, ring J can be heteroaryl;

Q is selected from the group consisting of O, S, NR^{13} , NR^{7A} wherein R^{7A} is the same as R^7 , CHR^{15} , $\text{X}^3\text{CH}(\text{R}^{15})$, and $\text{CH}(\text{R}^{15})\text{X}^3$, wherein X^3 is selected from the group consisting of $\text{BO}-$, $-\text{S}-$, $-\text{CH}_2-$, NR^{7A} , and NR^{13} ;

W is selected from the group consisting of CR^{18}R^7 and $[\text{CHR}^2] \text{CHR}^{50}$ where R^{50} is alkyl having from 1 to 4 carbons, $-\text{OH}$, alkoxy having from 1 to 4 carbons, $-\text{OC}(=\text{O})\text{R}^9$, $-\text{OC}(=\text{O})\text{NR}^{11}\text{R}^{12}$, $-\text{O}(\text{CH}_2)_p\text{NR}^{11}\text{R}^{12}$, $-\text{O}(\text{CH}_2)_p\text{OR}^{10}$, substituted or unsubstituted arylalkyl having from 6 to 10 carbons, and substituted or unsubstituted heteroarylalkyl;

R^{13} is selected from the group consisting of H, $-\text{SO}_2\text{R}^9$, $-\text{CO}_2\text{R}^9$, $-\text{C}(=\text{O})\text{R}^9$, $-\text{C}(=\text{O})\text{NR}^{11}\text{R}^{12}$, alkyl of 1-8 carbons, alkenyl having 2-8 carbons, and alkynyl having 2-8 carbons; and either

1) the alkyl, alkenyl, or alkynyl group is unsubstituted; or

2) the alkyl, alkenyl, or alkynyl group independently is substituted with 1 to 3 groups selected from the group consisting of aryl having from 6 to 10 carbons, heteroaryl, arylalkoxy, heterocycloalkoxy, hydroxylalkoxy, alkyloxy-alkoxy, hydroxyalkylthio, alkoxy-alkylthio, F, Cl, Br, I, $-\text{CN}$, $-\text{NO}_2$, $-\text{OH}$, $-\text{OR}^9$, $-\text{X}^2(\text{CH}_2)_p\text{NR}^{11}\text{R}^{12}$, $-\text{X}^2(\text{CH}_2)_p\text{C}(=\text{O})\text{NR}^{11}\text{R}^{12}$, $-\text{X}^2(\text{CH}_2)_p\text{OC}(=\text{O})\text{NR}^{11}\text{R}^{12}$, -

$X^2(CH_2)_pCO_2R^9$, $X^2(CH_2)_pS(O)_yR^9$, $-X^2(CH_2)_pNR^{10}C(=O)NR^{11}R^{12}$, $-OC(=O)R^9$, $-OCONHR^2$, $-O$ -tetrahydropyranyl, $-NR^{11}R^{12}$, $-NR^{10}CO_2R^9$, $-NR^{10}C(=O)NR^{11}R^{12}$, $-NHC(=NH)NH_2$, $NR^{10}C(=O)R^9$, $-NR^{10}S(O)_2R^9$, $-S(O)_yR^9$, $-CO_2R^2$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^2$, $-CH_2OR^{10}$, $-CH=NNR^{2A}R^{2A}$, $-CH=NOR^2$, $-CH=NR^9$, $-CH=NNHCH(N=NH)NH_2$, $-S(=O)_2NR^{2A}R^{2A}$, $-P(=O)(OR^{10})_2$, $-OR^{14}$, and a monosaccharide having from 5 to 7 carbons wherein each hydroxyl group of the monosaccharide is independently either unsubstituted or is replaced by H, alkyl having from 1 to 4 carbons, alkylcarbonyloxy having from 2 to 5 carbons, or alkoxy having from 1 to 4 carbons;

R^{15} is selected from the group consisting of H, OR^{10} , SR^{10} , R^{7A} , and R^{16} ;

R^{16} is selected from the group consisting of alkyl of 1 to 4 carbons; phenyl; naphthyl; arylalkyl having 7 to 15 carbons, $-SO_2R^9$, $-CO_2R^9$, $-C(=O)R^9$, alkyl having 1-8 carbons; alkenyl having 2 to 8 carbons, and alkynyl having 2 to 8 carbons, wherein

1) each alkyl, alkenyl, or alkynyl group is unsubstituted; or

2) each alkyl, alkenyl, or alkynyl group is substituted with 1 to 3 groups selected from the group consisting of aryl having from 6 to 10 carbons, heteroaryl, arylalkoxy, heterocycloalkoxy, hydroxylalkoxy, alkoxy-alkoxy, hydroxyalkylthio, alkoxy-alkylthio, F, Cl, Br, I, $-CN$, $-NO_2$, $-OH$, $-OR^9$, $-X^2(CH_2)_pNR^{11}R^{12}$, $-X^2(CH_2)_pC(=O)NR^{11}R^{12}$, $-X^2(CH_2)_pOC(=O)NR^{11}R^{12}$, $-X^2(CH_2)_pCO_2R^9$, $X^2(CH_2)_pS(O)_yR^9$, $-X^2(CH_2)_pNR^{10}C(=O)NR^{11}R^{12}$, $-OC(=O)R^9$, $-OCONHR^2$, $-O$ -tetrahydropyranyl, $-NR^{11}R^{12}$, $-NR^{10}CO_2R^9$, $-NR^{10}C(=O)NR^{11}R^{12}$, $-NHC(=NH)NH_2$, $NR^{10}C(=O)R^9$, $-NR^{10}S(O)_2R^9$, $-S(O)_yR^9$, $-CO_2R^2$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^2$, $-CH_2OR^{10}$, $-CH=NNR^{2A}R^{2A}$, $-CH=NOR^2$, $-CH=NR^9$, $-CH=NNHCH(N=NH)NH_2$, $-S(=O)_2NR^{2A}R^{2A}$, $-P(=O)(OR^{10})_2$, $-OR^{14}$, and a monosaccharide having from 5 to 7 carbons wherein each hydroxyl group of the monosaccharide is independently either unsubstituted or is replaced by H, alkyl having from 1 to 4 carbons, alkylcarbonyloxy having from 2 to 5 carbons, or

alkoxy having from of 1 to 4 carbons;

R^{18} is selected from the group consisting of R^2 , thioalkyl of 1-4 carbons, and halogen;

A^1 and A^2 are selected from the group consisting of H, H; H, OR^2 ; H, $-SR^2$; H, $-N(R^2)_2$; and a group wherein A^1 and A^2 together form a moiety selected from the group consisting of $=O$, $=S$, and $=NR^2$;

B^1 and B^2 are selected from the group consisting of H, H; H, $-OR^2$; H, $-SR^2$; H, $-N(R^2)_2$; and a group wherein B^1 and B^2 together form a moiety selected from the group consisting of $=O$, $=S$, and $=NR^2$; with the proviso that at least one of the pairs A^1 and A^2 , or B^1 and B^2 , form $=O$;

with the proviso that when Q is NH or NR^{7A} , and in any R^7 or R^{7A} group m is 0 and G is a bond, R^8 is H, and R^7 or R^{7A} contains one ring hetero oxygen atom at position A in a 5- or 6-membered ring, then B cannot be CHR^{17} where R^{17} is substituted or unsubstituted alkyl; and

with the further proviso that the compound of Formula I contains one R^7 or R^{7A} group or both an R^7 and R^{7A} group.

41. (Amended) The compound of claim 37 wherein the constituent variables of the compounds of Formula II are selected in accordance with [Table 8 *supra*] the following table:

| A1A2 | B1B2 | R3 | A | B | C | D | E | F |
|------|------|-------------------|-------|-----|------|------|------|-------|
| H2 | O | H | O | CH2 | bond | bond | bond | bond |
| H2 | O | H | O | CH2 | bond | bond | bond | bond |
| H2 | O | H | O | CH2 | bond | bond | bond | bond |
| H2 | O | H | C(OH) | CH2 | CH2 | bond | bond | bond |
| H2 | O | 3-Br | O | CH2 | bond | bond | bond | bond |
| H2 | O | 3-CH2OCH2-CH3 | O | CH2 | bond | bond | bond | bond |
| H2 | O | 3-CH2OCH2-CH2OCH3 | O | CH2 | bond | bond | bond | bond |
| H2 | O | H | O | CH2 | CH2 | CH2 | CH2 | bond |
| H2 | O | H | CH2 | O | CH2 | CH2 | CH2 | bond. |

64. (Amended) A pharmaceutical composition for treating [or preventing] prostate disorders comprising a compound of claim 1 and a pharmaceutically acceptable carrier.



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73. (Amended) A method for treating [or preventing] prostate disorders which comprises administering to a host in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1.

New claim 95 has been added.

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